

Leukemia and ABO Blood Group¹

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INTRODUCTION

RECENT INTEREST AND PROGRESS in the investigation of associations between disease incidence and ABO blood group have been summarised by Roberts (1957). The interpretation of such associations, when found, is difficult, but sufficient associations have been demonstrated by statistically sound methods that continued examination of these relationships seems indicated. In the present report, the results of examination of a series of 1387 patients with leukemia are recorded. Buckwalter and others (1956) and Steinberg (1957) have previously reported no evidence of association of leukemia with ABO blood group in studies of 456 patients with leukemia (all forms) and 459 patients with acute leukemia, respectively. The method of selection of one of the comparison samples in the present study may have relevance to studies of ABO groups in other diseases.

MATERIAL

The leukemia series which is the basis of the present study derives from two sources:

(1) An investigation, reported previously (MacMahon and Clark, 1956) of all Brooklyn residents diagnosed as leukemic in the years 1943–52. Blood group was recorded for 66 per cent (1127) of the 1709 total patients. The determination and recording of the blood group in most cases was prompted solely by the patient's need of transfusion, and consequently varied with the clinical course and type of leukemia. The 1127 patients are therefore not representative of the total 1709. For example, blood group was recorded for 69 per cent (529) of the 763 patients with acute leukemia, compared with 56 per cent (229) of the 411 patients with chronic lymphatic leukemia.

(2) All patients with leukemia attending five of the largest Brooklyn hospitals during the years 1953–56. Patients already known through inclusion in the 1943–52 series were excluded. Blood group was known for 76 per cent (260) of the 341 patients from this source.

Comparison samples were drawn from the alphabetical card files of the New York Regional Blood Program of the American Red Cross. These files at the time of sampling included a card for all donors from the New York area who had donated blood through the Red Cross since 1949. Two samples were drawn:

(1) Sample A. A systematic sample assembled by selecting cards at measured in-

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tervals throughout the alphabetical files. Only cards referring to residents of Brooklyn and to persons donating blood to this service for the first time were included. The sampling fraction was approximately 1 in 50.

(2) Sample B. A name-matched sample, assembled by selecting for each leukemia patient a donor of the same name. The variables matched were, in order, surname (1232 cases), sex (1121 cases), and first name (308 cases). Choice between several individuals of identical first and last name, where necessary, was on the basis of age matching. First donors were selected in preference to repeat donors, provided a matching surname was obtained. Of the 1232 cases in which the surname could be matched, 1168 were matched by first donors and 64 repeat donors. The donor files contained no donors with surnames to match eleven per cent (155) of the 1387 leukemia patients.

COMPARISON WITH SAMPLE A

The distributions by blood group of the two leukemia series and of the systematic comparison sample are shown in table 1. Since there is no significant difference between the distributions of the two leukemia series, they are combined in subsequent examinations.

The combined leukemia series shows, relative to the comparison sample, a deficiency of group O patients and an excess of groups B and AB. The difference between the two distributions is statistically highly significant. The difference could be accounted for by:

(1) A tendency for leukemia to occur less frequently in persons of group O than in persons of groups B and AB.

(2) A difference between the ethnic compositions of the two series. Such a difference might arise either through ethnic variation in leukemia incidence or because the leukemia series and the blood donor sample were not drawn from the same parent population, i.e. were not representative of the Brooklyn population.

Two ethnic associations of leukemia incidence in the area of the present study have been recognized (MacMahon and Koller, 1957). These are, a low incidence in the

TABLE 1. DISTRIBUTION BY ABO BLOOD GROUP OF 1387 PATIENTS WITH LEUKEMIA, AND A SYSTEMATIC SAMPLE OF BLOOD DONORS (SAMPLE A), BROOKLYN, 1943-56

Blood group	Leukemia Series						Blood donor sample A	
	1943-52		1953-56		Total		Number	Per cent
	Number	Per cent	Number	Per cent	Number	Per cent		
O	458	40.6	103	39.6	561	40.4	900	45.8
A	417	37.0	102	39.2	519	37.4	728	37.0
B	179	15.9	44	16.9	223	16.1	261	13.3
AB	73	6.5	11	4.2	84	6.1	78	4.0
Total	1127	100.0	260	99.9	1387	100.0	1967	100.1

Comparison of the two leukemia series:

$$\chi^2 = 1.2, n = 3, 0.7 < p < 0.8$$

Comparison of the total leukemia series and the blood donor sample:

$$\chi^2 = 16.9, n = 3, p < 0.001$$

Negro compared to the white population, and a higher rate in the Jewish white population than in non-Jewish whites. The first association is not likely to affect the blood group comparison, since the Negro population of Brooklyn is low (about 7 per cent) and the difference between Negroes and whites in leukemia rates is relatively small (1 to 1.3). However, the second ethnic association of leukemia incidence could well account for differences in ABO distributions. The leukemia rate in the Jewish population is perhaps twice that in the non-Jewish groups, and approximately 35 per cent of the population of the Borough is of Jewish ancestral background. Furthermore, there is, as shown in Table 2, a difference in blood group distribution between the Jewish and non-Jewish leukemia patients. This difference is in the direction necessary to explain the difference between the leukemia series and the comparison sample on the basis of a higher representation of Jews in the leukemia series—that is, compared to the non-Jewish patients, the series of Jewish patients is relatively deficient in persons of group O.

In table 2, the religious affiliation is as recorded by the patient on admission to hospital. Ethnic associations cannot be examined directly in the sample of blood donors, since Red Cross policy precludes the recording of color, religion or other indicators of ancestral background. However, in this area, an idea of ancestral background is frequently suggested by the surname. For 923 of the 1967 donors in Sample A it was considered that the surname was either definitely Jewish or definitely not Jewish (mostly Italian and Irish); 1044 could not be definitely classified. Blood

TABLE 2. DISTRIBUTION OF WHITE PATIENTS WITH LEUKEMIA ACCORDING TO RELIGION AND ABO BLOOD GROUP

Blood group	Jewish		Catholic and Protestant	
	Number	Per cent	Number	Per cent
O	226	34.0	291	45.5
A	261	39.2	235	36.8
B	120	18.0	90	14.1
AB	58	8.7	23	3.6
Total	665	99.9	639	100.0

Religion was unknown for 13 patients.

$\chi^2 = 28.4$, $n = 3$, $p < 0.001$.

TABLE 3. PERCENTAGE DISTRIBUTION OF BLOOD DONOR SAMPLE A ACCORDING TO ABO BLOOD GROUP AND PRESUMED ANCESTRAL BACKGROUND AS JUDGED FROM LAST NAME

Blood group	Names classified as				Total classified		Names not classified	
	Jewish		Non-Jewish					
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
O	142	37.9	281	51.3	423	45.8	477	45.7
A	165	44.0	184	33.6	349	37.8	379	36.3
B	46	12.3	62	11.3	108	11.7	153	14.7
AB	22	5.9	21	3.8	43	4.7	35	3.4
Total	375	100.1	548	100.0	923	100.0	1044	100.1

$\chi^2 = 17.3$, $n = 3$, $p < 0.01$.

group was not known by the person classifying the names. The distributions are shown in Table 3. Once again the marked deficiency of group O in the Jewish group is evident. A considerable relative excess of group A is also seen in the group presumed Jewish.

COMPARISON WITH SAMPLE B

Comparison of the distribution of the Jewish leukemia patients (table 2) with that of the blood donors with Jewish names (table 3), or of the non-Jewish leukemia patients with the blood donors with non-Jewish names would be unsatisfactory since the criteria of ethnic background are different in the samples being compared. A second sample (B) was therefore selected from the blood donor files. Since it was not possible to match this sample with any more reliable index of ethnic background, an attempt was made to match it with the surnames of the leukemia series, as described above. From over 600,000 cards in the blood donor files, it was possible to find a surname match for 88 per cent (1232) of the 1387 leukemia patients. This type of matching, insofar as it is a satisfactory index of ethnic background, will reduce differences between the leukemia and blood donor samples which may result from differences between ethnic groups in frequency of blood donation, as well as those due to ethnic differences in leukemia incidence.

The distributions of the 1232 leukemia patients and their name-matched blood donors are shown in table 4. There is no significant difference between the two distributions. It is concluded that the differences between the leukemia series and the systematic sample of blood donors results from differences between the two series in ethnic representation—probably in relative representation of patients of Jewish ancestral background. This difference probably results from the high incidence of leukemia in the Jewish population of Brooklyn.

TYPE OF LEUKEMIA, AND RH STATUS

The distribution of leukemia patients according to ABO blood group in diagnostic categories is shown in table 5. There is no evidence of statistically significant heterogeneity. The pattern of blood group distribution is more unusual for the 295 patients with chronic granulocytic leukemia than for any of the other major diagnostic categories. However, the distribution of the chronic granulocytic cases does not differ significantly from the distribution of patients with all other diagnoses ($\chi^2 = 5.4$,

TABLE 4. DISTRIBUTION OF 1232 LEUKEMIA PATIENTS AND A NAME-MATCHED SAMPLE OF BLOOD DONORS (SAMPLE B), ACCORDING TO ABO BLOOD GROUP

Blood group	Leukemia patients		Name matched blood donors	
	Number	Per cent	Number	Per cent
O	507	41.2	507	41.2
A	455	36.9	493	40.0
B	193	15.7	166	13.5
AB	77	6.3	66	5.4
Total	1232	100.1	1232	100.1

$\chi^2 = 4.4$, $n = 3$, $0.2 < p < 0.3$.

TABLE 5. DISTRIBUTION ACCORDING TO TYPE OF LEUKEMIA AND ABO BLOOD GROUP

Blood group	Acute		Chronic		Subacute and other	Total
	Granulocytic	Other	Granulocytic	Lymphocytic		
O	159	121	102	108	71	561
A	144	102	120	106	47	519
B	66	35	53	48	21	223
AB	15	13	20	23	13	84
Total	384	271	295	285	152	1387

$$\chi^2 = 18.6, n = 12, p \approx 0.1.$$

TABLE 6. DISTRIBUTION OF LEUKEMIA SERIES AND COMPARISON SAMPLES ACCORDING TO Rh STATUS

Type of leukemia	Number		Total	Per cent Rh negative
	Rh neg.	Rh pos.		
Acute granulocytic	280	25	305	8.2
Other acute forms	188	21	209	10.0
Chronic granulocytic	210	23	233	9.9
Chronic lymphocytic	202	25	227	11.0
Other	101	15	116	12.9
Total	981	109	1090	10.0
Comparison sample A	1747	220	1967	11.2
Comparison sample B	1083	149	1232	12.1

$n = 3, 0.1 < p < 0.2$). It would nevertheless seem desirable to record further data, when available, on the comparison of the ABO distributions of series of leukemia patients according to specific type of leukemia.

Distributions according to Rh status are recorded in table 6. There are no significant differences between the percentages of Rh negative patients in any of the groups examined.

DISCUSSION

The most obvious deficiency of the present study is the possibility of bias arising from the fact that data on blood group were obtained for only 68 per cent of the total series of leukemia patients. However, to affect the results of the examination it would be necessary for the probability of transfusion (and hence of recording of blood type) to be related to ABO group. The material has been examined for evidence of variation between patients of different blood groups in the duration of symptoms prior to diagnosis and in the clinical nature of the presenting symptoms. No such variation was evident. No relationship was found between ABO blood group and the length of survival of patients with the acute leukemias (MacMahon and Forman, 1957). For the chronic leukemias it was noted that duration is significantly longer for patients of group B than for patients of other groups (Feinleib and MacMahon, 1958). However, it is difficult to see how this latter finding could affect the specific results noted in the present study.

Of incidental interest to the negative findings in the leukemia data, are the differences in blood group distribution noted between the Jewish and non-Jewish populations of Brooklyn, and the fact that these differences are readily detectable when surname is used as an index of ethnic background. Roberts (1942) noted differences in blood group distribution on the basis of surname in Wales. The possibility exists of using surname matching, as here described, to differentiate blood group associations of disease occurring secondary to ethnic associations from those more directly related to blood group. This method, if practicable, would be less time consuming than the sibship studies as used by Clarke et al. (1956). However, the applications of surname matching are obviously limited to the examination of ethnic associations which are clearly indicated by surname, and to geographic areas and time periods in which such surname-identification persists. It should be noted in addition that sibship studies also provide a mechanism of elimination of maternal effects and non-racial stratification not provided by surname matching.

SUMMARY

Data are recorded on the ABO blood group of 1387 patients with leukemia diagnosed in Brooklyn between 1943 and 1956. By comparison with a systematic sample of Brooklyn blood donors, the leukemia series was deficient in persons of group O. It was noted, however, that both in the leukemia series and in the blood donor sample there was a lower percentage of patients of group O among Jewish than among non-Jewish groups. Since leukemia is twice as frequent in the Jewish as in the non-Jewish population of Brooklyn, this is a ready explanation of the relative deficiency of persons of group O in the leukemia series. This explanation is supported by the observation that the distribution of the leukemia series by ABO blood group did not differ significantly from that of a sample of blood donors matched to the surnames of the leukemia patients.

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